

Amendment and Response Under 37 CFR §1.116

Serial No.: 09/884,894

Filed: June 19, 2001

Title: BIFIDOBACTERIA AND SIDEROPHORES PRODUCED THEREBY AND METHODS OF USE

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### Remarks

The Office Action mailed May 20, 2003 has been received and reviewed. Claims 29, 41, 43, and 44 having been amended, the pending claims are claims 9-15 and 20-44. Claims 9-15, 20-28, 30-40, and 42 have been withdrawn from examination by the Examiner, such that claims 29, 41, 43, and 44 are presently under examination. Reconsideration and withdrawal of the rejections are respectfully requested.

The amendment of claims 29, 41, and 43-44 to recite "isolated" is supported by the specification at, for instance, page 10, lines 10-12. This amendment is made to clarify that the *Bifidobacterium* has been removed from its natural environment and grown as a biologically pure culture. The amendment to recite "inhibits growth a *Lactococcus lactis*" is supported by the specification at, for instance, Example 2.

### Interview Summary

Examiners Ware and Naff are thanked for the courtesies extended during the telephone interview on July 17, 2003.

### Rejection under 35 U.S.C. §132

The Examiner rejected deleting the terms "decreased" and "reduced" to replace them with "increased." This rejection is respectfully traversed.

It is applicant's position that amending the terms "decreased" and "reduced" to recite "increased" at page 11, lines 17 and 19, does not introduce new matter into the disclosure of the invention, and instead corrects an obvious error. The original wording of the specification stated that the replication of a microbe is considered to be inhibited when its doubling time is decreased. This is an obvious error, as the inhibition of replication of a microbe results in fewer cell divisions, which is an *increase* in doubling time, and not a decrease. The inhibition of replication of a microbe could not result in a decrease in doubling time. Thus, it would be readily recognized by a skilled person that the term "increased" was intended.

The Examiner is respectfully requested to reconsider and withdraw the rejection under 35 U.S.C. §132.

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### **The 35 U.S.C. §112, First Paragraph, Rejection**

The Examiner rejected claims 29, 41 and 43-44 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for Bifidobacterium strains RecB1, strain RecB4, strain J1, strain J2, strain J4, strain P1, strain 6A or strain 10A, does not reasonably provide enablement for any and all strains of Bifidobacterium. This rejection is respectfully traversed.

In addition to the comments made by the applicant in the Response mailed to the Office February 21, 2003, the Examiner is requested to consider the following. The Examiner has based this rejection on the assertion that "the unpredictability in the microbiological arts is very high and one of skill in the art would not be capable of predicting which Bifidobacterium strain produces a siderophore" (Action, page 3). As evidence to support this assertion of unpredictability, the Examiner refers to Yildirim (J. Food Prot., 61(1):47-51 (1998)) "as art against the claim clearly teach[ing] that not all strains of Bifidobacterium secrete or form siderophores" (Action, page 4). Specifically, the Examiner states that "the undue burden of experimentation to select for appropriate strains which can produce siderophores is very high, because the cited prior art clearly shows that not all strains can produce siderophores" (Action, page 4).

As discussed below in the response to the art-based rejections, Yildirim et al. do not teach or suggest the siderophore recited in the present claims. Since Yildirim et al. do not teach or suggest the siderophore recited in the present claims, Yildirim et al. cannot be used by the Examiner to support the argument for unpredictability put forth in the Action.

The applicant strenuously disagrees with the reasoning leading to the conclusion that the level of unpredictability in the art is so high that undue experimentation is required. "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (citation omitted). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims (citations omitted)." In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The entire argument for concluding that undue experimentation is required is based on factor 7. The other factors have not been considered,

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and as stated in the M.P.E.P., "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole" (M.P.E.P. §2164.01(a)). The Examiner is requested to consider all the evidence related to each of these factors.

With respect to the factors listed above, the Examiner is respectfully requested to note that the specification discloses working examples teaching how to isolate and identify *Bifidobacterium* strains that secrete a siderophore. Working example 1 discloses how *Bifidobacterium* strains were isolated. The specification further discloses at working example 2 the method used for detecting siderophore production by bifidobacteria. It is evident upon review of the working examples that the quantity of experimentation needed to make or use the invention based on the content of the disclosure is minimal, and essentially all of the experimentation required is provided by the inventor. Further, as admitted by the Action, "methods of screening bacteria are conventional in the art . . ." (Action, page 3), thus the experimentation required is well within the level of one of ordinary skill. The applicant does not agree with the Examiner's assertion that "the unpredictability in the microbiological arts is very high . . ." (Action, page 3). However, even if this assertion was true, the guidance and direction provided by the applicant is more than needed to enable the invention.

Furthermore, the Examiner is requested to consider the Rule 132 Declaration of Dr. Daniel O'Sullivan as evidence that the present application enables the identification of bifidobacteria that produce a siderophore. In his Declaration, Dr. O'Sullivan states that the methods described in the present application were used to isolate multiple bifidobacteria from 10 individuals. One bifidobacteria was chosen from each individual for further analysis, and each of the 10 chosen bifidobacteria produced a siderophore. As stated by Dr. O'Sullivan, the data in the Declaration are proof that the skilled person can easily obtain bifidobacteria strains and determine if they produce a siderophore, and that each time the experimental procedure was conducted with a subject, a bifidobacteria producing a siderophore was obtained.

It is respectfully submitted that the Declaration provides evidence that a person of ordinary skill in the art could, using the present application as a guide and the knowledge

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generally available to the skilled person, practice the claimed invention commensurate in scope with the claims.

Reconsideration and withdrawal of the rejection of claims 29, 41 and 43-44 under 35 U.S.C. §112, first paragraph, is respectfully requested.

**Rejections under 35 U.S.C. §102 and §103**

*The Yildirim et al. document*

The Examiner rejected claims 29, 41 and 43-44 under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Yildirim et al., for those reasons of record. The rejection is respectfully traversed.

According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." The present claims recite "a siderophore that inhibits growth of a *Lactococcus lactis*" (claims 29, 41, 43, and 44). Yildirim et al. teach a Bifidobacterium that produces a bacteriocin referred to as bifidocin B. The Action asserts that this bifidocin B is a siderophore (see Action at paragraph bridging pages 4-5). Applicant respectfully continues to disagree with this assertion. The inhibitory activity of bifidocin B against bacteria was determined by the authors and was found to *not* inhibit *Lactococcus lactis* (see Yildirim et al. at the paragraph bridging pages 48 and 49, and Table 1 at page 49). In contrast, the pending claims recite "a siderophore that inhibits growth of a *Lactococcus lactis*." Thus, Yildirim et al. do not disclose each and every element as set forth in the claims. Accordingly, Yildirim et al. do not anticipate the pending claims.

The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 29, 41, and 43-44 under 35 U.S.C. §102(b) over Yildirim et al.

Regarding the rejection of claim 29, 41, and 43-44 under 35 U.S.C. §103(a) as obvious over Yildirim et al., the burden is on the Office to establish a *prima facie* case of nonobviousness of the claimed invention. The three criteria that must be met (MPEP § 2143) are: (i) there must be a suggestion or motivation to modify the reference; (ii) there must be a reasonable expectation

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of success; and (iii) the prior art reference must teach or suggest all the claim limitations. It is respectfully submitted that the Office has not met this burden.

The Action does not provide any motivation for modifying the cited document, or any indication as to why there would be a reasonable expectation of success. Further, since the cited document does not teach or suggest a composition including a Bifidobacterium that secretes a siderophore that inhibits growth of a *Lactococcus lactis* (claims 29 and 41) or including a Bifidobacterium that can secrete a siderophore that inhibits growth of a *Lactococcus lactis* (claims 43 and 44), not all the claim limitations are present. The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 29, 41, and 43-44 as obvious over Yildirim et al.

*The Nisbet et al. document*

The Examiner rejected claims 29, 41 and 43-44 as being anticipated by Nisbet et al. (U.S. Patent No. 5,340,577) for reasons of record. The rejection is respectfully traversed.

The present invention is directed to a composition including "a Bifidobacterium that secretes a siderophore that inhibits growth of a *Lactococcus lactis*" (claims 29 and 41) or including "a Bifidobacterium that can secrete a siderophore that inhibits growth of a *Lactococcus lactis*" (claims 43 and 44). Nisbet et al. disclose a probiotic effective for controlling Salmonella colonization of fowl (Nisbet et al., col. 3, lines 17-18). "Suitable bacteria utilized in the probiotic include substantially biologically pure bacteria of the genera *Lactobacillus*, *Enterococcus*, *Bifidobacterium*, *Propionibacterium* and *Escherichia*, in combination with one or both of *Lactococcus lactis* and *Citrobacter freundii*" (Nisbet et al., col. 3, lines 27-29). Nisbet et al. also disclose that "[t]he bacteria also should not produce bacteriocins effective against the other above-mentioned bacteria of the probiotic" (Nisbet et al., col. 3, lines 55-57). This latter statement is proof that a bacterium in the probiotic should *not* inhibit growth of the other bacteria of the probiotic. If the Bifidobacterium taught by Nisbet et al. secreted a siderophore that inhibits growth of *Lactococcus lactis*, the Bifidobacterium would inhibit the growth of other bacteria of the Nisbet et al. probiotic. Moreover, Nisbet et al. state that when all eleven isolates described in Example 1, including a *Lactococcus lactis*, were combined and grown together, all eleven strains were subsequently isolated again (see paragraph spanning col. 9-10) thereby

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showing that the Bifidobacterium taught by Nisbet et al. does not inhibit the growth of *Lactococcus lactis*. Thus, the Bifidobacterium of Nisbet et al. do not secrete a siderophore that inhibits growth of *Lactococcus lactis*. As Nisbet et al. do not disclose each and every element as set forth in the claims, Nisbet et al. do not anticipate the pending claims.

The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 29, 41, and 43-44 under 35 U.S.C. §102(b) over the cited document.

The Examiner rejected claims 29, 41 and 43-44 under 35 U.S.C. §103(a) as being unpatentable over Nisbet et al. in view of Yildirim et al. This rejection is respectfully traversed.

It is respectfully submitted that the Office has not met the burden of establishing a *prima facie* case of obviousness.

The Action does not provide any motivation for modifying the cited documents, or any indication as to why there would be a reasonable expectation of success. Further, since the cited documents do not teach or suggest a composition including a Bifidobacterium that secretes a siderophore that inhibits growth of a *Lactococcus lactis* (claims 29 and 41) or including a Bifidobacterium that can secrete a siderophore that inhibits growth of a *Lactococcus lactis* (claims 43 and 44), not all the claim limitations are present. The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 29, 41, and 43-44 as obvious over Nisbet et al. in view of Yildirim et al.

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### Summary

It is respectfully submitted that the pending claims 29, 41, 43, and 44 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

#### CERTIFICATE UNDER 37 C.F.R. 1.8:

The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, Mail Stop AF, P.O. Box 1450, Alexandria, VA 22313-1450, on this 22nd day of September, 2003, at 4:30 pm (Central Time)

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Respectfully submitted,

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